

## Comparison of New ARDS Criteria (Berlin) with Old Criteria (AECC) and its Application in Country with Limited Facilities

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### Abstract

Acute Respiratory Distress Syndrome (ARDS) is defined as an acute inflammatory syndrome that accompanied with increased permeability of the alveolar-capillary membrane. Some ARDS diagnostic criteria had been made throughout years, such as American-European Consensus Conference (AECC) criteria. The newest one, the Berlin criteria, was published in 2012. The Berlin criteria excludes the utilization of pulmonary artery catheter to measure pulmonary wedge pressure. The utilization of Berlin Criteria is expected to be easier to used in country with limited facilities compares to previous criteria.

**Keywords:** Acute respiratory distress syndrome, Berlin, AECC, Criteria, Comparison, Limited facilities country

### Some ARDS Definitions

In 1821, Laennec found a condition characterized by pulmonary edema that occurred without heart failure. Some terms were tried to describe the syndrome, such as double pneumonia, post-traumatic lung, and shock lung [1]. The term Acute Respiratory Distress Syndrome (ARDS) was first declared by Asbaugh, et al. in 1967. Acute respiratory distress syndrome diagnosis was made based on five clinical features: associated risk factor, severe hypoxemia despite adequate oxygen supplementation, bilateral infiltrates on chest xray, decreased lung compliance, and no evidence of congestive heart failure [2].

Another definition of ARDS was made in 1988 which included 4 aspects that contribute to respiratory injury: positive end expiratory pressure (PEEP),  $\text{PaO}_2/\text{FiO}_2$  ratio, lung compliance, and infiltrates on chest xray. Each item was designated a score from 1 to 4 points, and ARDS diagnosis is made if the total score is more than 2.5. This criteria was named the Lung Injury Score (LIS) [3,4]. This criteria had some disadvantages, such as low specificity (no consideration regarding risk factor, possibility of cardiogenic pulmonary edema included as an etiology of ARDS) and uncontrolled prognostic validity [5].

In 1994, a new definition was declared by American-European Consensus Conference (AECC), with the criteria of severe hypoxemia including  $\text{PaO}_2/\text{FiO}_2$  ratio less than 200 mmHg, bilateral infiltrates on chest xray, and no evidence of cardiogenic pulmonary edema. However, implementation of this criteria had many limitations [6].

There have been several studies that compared some ARDS diagnostic criteria. Moss, et al. in 1995 compared the LIS, modified LIS, and AECC criteria. The results show that they identified similar ARDS patients [7]. Goh et al. in 1998 compared LIS with the AECC criteria. The results show that both criteria identified a similar group of ARDS patients [4]. Niall, et al. in 2005, compared the diagnostic accuracy of three ARDS diagnostic criteria. They are AECC criteria, LIS, and Delphi definition. The study showed that ARDS was under-diagnosed by the clinicians [8].

### AECC Criteria

AECC coined the new definition of ARDS and ALI (Acute Lung Injury). ARDS was characterized by acute hypoxemia ( $\text{PaO}_2/\text{FiO}_2$  ratio less than 200 mmHg) with bilateral infiltrates seen on chest xray and no evidence of left atrial hypertension. On the other hand, ALI had a similar criteria to ARDS, but with a lesser degree of hypoxemia ( $\text{PaO}_2/$

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FiO<sub>2</sub> ratio less than 300 mmHg) [9]. ALI was defined as an acute inflammatory syndrome that accompanied with increased permeability of the alveolar-capillary membrane. The cutoff value to differentiate ALI and ARDS is 200 mmHg [3].

Hydrostatic pulmonary edema was excluded from the diagnostic criteria of ARDS because the pattern of gas exchange and appearance in chest xray could be similar to ARDS. PEEP value was not included in this criteria because it is inconsistent and time dependent [3]. Actually, ALI was a general term for ARDS patients (PaO<sub>2</sub>/FiO<sub>2</sub> ratio less than 200 mm Hg) and patients with a PaO<sub>2</sub>/FiO<sub>2</sub> ratio of 200 to 300 mmHg. In daily practice, the definition caused disagreements and confusion among clinicians. Many clinicians used the term ALI for patients with a PaO<sub>2</sub>/FiO<sub>2</sub> ratio of 200 to 300 mmHg. [3,5].

After the application of this criteria for 18 years, there were still many questions left unanswered such as definition of the term 'acute' that is not clearly described, sensitivity of the PaO<sub>2</sub>/FiO<sub>2</sub> ratio that was inconsistent (depend on the setting of ventilator), poor reability of chest Xray, and difficulties in distinguishing the existence of hydrostatic pulmonary edema [9].

## The Berlin Criteria

The AECC criteria had been used widely for diagnosing ARDS. Many criticisms had been made toward this criteria. In 2012, a panel of experts from The European Society of Intensive Care Medicine, the American Thoracic Society, and the Society of Critical Care Medicine had revised the ARDS definition. The panel had agreed to the earlier concept of ARDS as an acute syndrome with diffuse lung infiltrates, edema caused by increased alveolar-capillary membrane permeability, and decreased oxygenation. The Berlin definition explained the definition of acute onset, classification of decreased oxygenation, minimum level of PEEP, new imaging definition, and exclusion of hydrostatic pulmonary edema [3,10].

There were some differences between the Berlin criteria and the previous ARDS criteria, including definition of acute, classification of oxygenation, minimum level of PEEP, imaging definition, and exclusion of hydrostatic pulmonary edema. The Berlin definition stated that maximum period between risk factor exposure and ARDS development is 7 days. The choice of 7 days was made because nearly all patients developed it within 7 days after exposure to the risk factor. The risk factors of ARDS were classified into direct and indirect risk factors. Direct risk factors (direct lung injury) include pneumonia, aspiration of gastric contents, inhalation injury, pulmonary contusion, lung vasculitis, and drowning while non-pulmonary sepsis, multiple trauma, pancreatitis, non cardiogenic shock, drug overdose, and TRALI (Transfusion associated acute lung injury) classified as indirect risk factors (indirect lung injury) [11,12].

The Berlin criteria declared new classification of ARDS; PaO<sub>2</sub>/FiO<sub>2</sub> ratio ≤300 and >200 is mild ARDS; PaO<sub>2</sub>/FiO<sub>2</sub> ratio 100-200 is moderate ARDS; PaO<sub>2</sub>/FiO<sub>2</sub> ratio <100 is severe ARDS [13]. In this new criteria, the minimum level of PEEP required for diagnosing ARDS is 5cmH<sub>2</sub>O. This value excludes hypoxemia caused by atelectasis.

Imaging criterion of ARDS is bilateral infiltrate on chest Xray that can not be explained by effusion, collapsed lung, or lung nodule [13]. Additionally, imaging can be derived from thorax CT

scan instead of chest Xray.<sup>3</sup> Computer tomography will reveal a heterogeneous bilateral pumunary infiltrate mainly in gravity-dependent lung regions [14].

Moreover, according to the Berlin definition, the pulmonary artery wedge pressure criterion is removed. Clinical judgement is adequate to exclude hydrostatic pulmonary edema in the presence of ARDS risk factor. If the risk factor can not be identified, further evaluation, such as achocardiography, is needed to be performed.

The Berlin definition has a better predictive validity for mortality compared to the AECC criteria [9]. A study by Arnaud, et al. in 2013 showed that the Berlin criteria could identify severe ARDS of more than 72 hours among patients with DAD (diffuse alveolar damage). DAD is a hallmark of ARDS, characterized by hyaline membrane, edema, cell necrosis, or fibrosis [6,15]. Whereas a study by Pinheiro et al in 2007 among autopsy patients showed that AECC criteria was less accurate to identify ARDS [16]. Another study conducted by Kao, et al. showed that DAD was found in 56,4% ARDS patients based on Berlin definition and who underwent open lung biopsy [17]. However, different result showed by a study conducted by Aisiku, et al. This study showed comparison of the Berlin and the AECC definitions did not give significant differences in incidence or associated mortality attributable to ARDS in severe TBI (traumatic brain injury) patients [18].

The Berlin definition is a major step for a uniform classification of ARDS [19]. In general, determination if an individual fulfills a specific criteria for ARDS does not change the outcome. However, application of the Berlin criteria to diagnose ARDS, or any other criteria, may lead to underdiagnosis of the milder form of ARDS [20].

Implementation of the Berlin criteria in developing countries, or in a country with limited facilities, can be beneficial. The Berlin criteria rules out utilization of a pulmonary artery catheter to measure the pulmonary wedge pressure. A patient can be diagnosed with ARDS if the respiratory failure is not caused by heart failure or fluid overload, as based on clinical judgement [9]. Moreover, patients with PaO<sub>2</sub>/FiO<sub>2</sub> ratio ≤300 are diagnosed with ARDS in Berlin criteria. Earlier ARDS diagnosis can be made compared to AECC criteria. Earlier diagnosis allows earlier management of the ARDS patient, hence it can increase the survival of ARDS patients as a consequence.

For further consideration, ARDS is a syndrome, not a disease. Survival depends on identification of the etiology rather than any form of specific organ support. Development of better strategies in the future to diagnose ARDS is considered, such as with specific biomarker of inflammation, disordered coagulation, and alveolar-capillary membrane disruption, rather than using a clinical criteria alone [20,21]. For example, procalcitonin can predict the mortality of ARDS patient caused by severe CAP [22]. Another specific biomarker is needed to diagnose ARDS. A study conducted by Ozolina et al in 2016 shows that increased plasma level of tissue factor and plasminogen activator inhibitor-1 might support to diagnose ARDS in after-7-days ventilated patients in ICU [23].

In conclusion, the Berlin criteria excludes the utilization of pulmonary arthery catheter to measure pulmonary wedge pressure. Consequently, the application of this criteria in country with limited facilities is expected to give more benefits compared

to previous criteria. Further study is needed to prove the benefit of the Berlin criteria implementation in developing countries.

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